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의학석사 학위논문

Sudden sensorineural hearing loss in children
: clinical characteristics and age-related prognosis

소아 돌발성 난청
: 임상적 특성과 연령에 따른 예후

2017 년 2 월

서울대학교 대학원

임상의과학과

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ABSTRACT

Sudden sensorineural hearing loss in children : clinical characteristics and age-related prognosis

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Background and objectives: Although many studies have investigated sudden sensorineural hearing loss (SSNHL) in adults, there are few studies on SSNHL in the pediatric population; research on treatment and prognosis in this area is limited. The aim of this study was to evaluate clinical characteristics, treatment outcomes and prognostic factors in children with SSNHL.

Methods: A retrospective review of medical records of 67 pediatric patients (67 ears) in three hospitals of Seoul National University from January 2005 to August 2016 was performed to analyze patients' clinical manifestations and audiograms. All patients were treated with high-dose systemic prednisolone (1 mg/kg), and intratympanic steroid injection was done in 17 patients. Audiologic evaluation was carried out after treatment according to Siegel's criteria, and hearing recovery was defined as complete recovery and partial recovery. Patients were divided into two groups: childhood group (ages between 4 and 12 years old) and adolescent group

(age > 12 years), and clinical characteristics and treatment outcomes were investigated. In addition, patients were divided into two groups according to hearing recovery, and evaluation was made regarding possible prognostic factors.

Results: The recovery rate in the 67 patients was 55.2%. The recovery rate of the childhood group was significantly lower than that of the adolescent group (*p=0.038*). While presence of vertigo did not significantly correlate with prognosis (*p=0.430*), presence of tinnitus was significantly associated with hearing recovery (*p=0.007*). Audiologic assessment revealed that a low initial hearing threshold, high speech discrimination score and descending type of audiogram were positively associated with hearing recovery (*p=0.002, p=0.003 and p=0.029*, respectively). The route of steroid administration was not significantly related to prognosis (*p=0.205)*, and intratympanic steroid injection had no significant effect on treatment outcome (*p=0.187*). Cochlear enhancement on magnetic resonance imaging was found in 6 patients among 45 patients who had inner ear magnetic resonance imaging.

Conclusion: The childhood group had worse treatment outcomes than the adolescent group. High initial hearing threshold and absence of tinnitus were poor prognostic factors of hearing recovery. Active treatment is required for patients with these poor prognostic factors and childhood patients with SSNHL.

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keywords : Sudden sensorineural hearing loss, children, pediatric, age, prognosis

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Figure 3. Comparison of recovery rates according to cochlear enhancement on MRI (n = 45). Recovery rates in patients with cochlear enhancement and those without cochlear enhancement were 33.3% and 56.4%, respectively.

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is defined as rapidly developing hearing loss within less than three days, and the level of the hearing loss is more than 30 dB in at least three consecutive frequencies.[1] It is regarded as an otologic emergency, because it can cause a permanent hearing loss and psychologic sequelae if not treated immediately. In the United States, the incidence of SSNHL has been reported to be 27 per 100,000 per year.[2] However, some authors have suggested that the incidence of SSNHL might be much higher than the figures previously reported.[3] Bilateral SSNHL is infrequent, and concurrent bilateral involvement is very rare.[4] SSNHL commonly occurs in patients aged between 25 and 60 years old, with a peak in prevalence for patients between 46 and 49 years old.[5,6] SSNHL in children is very rare and its cause is still unclear. It has been reported that 6.6% of patients with SSNHL were under 18 years of age, 3.5% under 14 years, and only 1.2% under 9 years.[7] Due to the rarity of SSNHL in the pediatric population, research regarding etiology, treatment outcomes, and prognosis of SSNHL in children is limited. Although most SSNHL is idiopathic, potential causes including infection, autoimmune, or neoplasm can be identified in some patients with SSNHL. In a meta-analysis, the identified causes of sudden-onset hearing loss were infection (13%), otologic disease (6%), trauma (4%), vascular or hematologic disease (3%), neoplasm (2%), and other (2%).[8] Possible causes of SSNHL in a pediatric population are somewhat different from those in an adult

population.[9] Congenital anomalies of the inner ear should be considered, and infections with several viruses including cytomegalovirus (CMV), Epstein-Barr virus, or mumps virus can be causative agents in children with SSNHL; however, the most of children with SSNHL have seronegative results for these viruses.

Several studies have shown hearing recovery rates of 32% to 65% (average 46.7%) without treatment, typically within 2 weeks of onset; medical treatment including steroids is known to improve hearing recovery.[4,10,11] Systemic steroids are the mainstay treatment for SSNHL on the basis of anti-inflammatory effect.[11] Recently, intratympanic steroid injection is being increasingly used in the treatment of SSNHL. Although optimal dose and the mechanism remain unknown, a higher concentration of steroids in the inner ear may be associated with the hearing recovery.[12] Several studies have shown the potential benefits of using intratympanic steroid injection as a salvage therapy.[13,14] In contrast to SSNHL in adults, however, treatment guidelines in children have not been established.[1]

Some studies have shown that the prognosis in children with SSNHL is worse than that in adults.[4,15] Because children grow rapidly with time, in addition, a pediatric population will have large developmental variability according to age, and different prognosis can be present among the children due to this variability. However, there are few studies of the prognosis of SSNHL according to age in a homogenous pediatric population, and the results are controversial.[16,17] Prognostic factors such as patient age, pattern of audiogram, presence of vertigo at onset and

late initiation of treatment have been reported in large adult populations with SSNHL.[4,18-20] Due to its low incidence, there have been few studies regarding prognostic factors in homogenous pediatric populations.[15,21] The aims of this study were to analyze clinical and audiologic characteristics associated with prognosis in children with SSNHL and investigate age-related treatment outcomes in a pediatric population.

MATERIALS AND METHODS

Study Design and Patients

We performed a retrospective medical record review of SSNHL patients in three large medical centers from January 2005 to August 2016 and identified 67 patients aged between 4 and 19 years. These 67 patients were divided into two groups: childhood group (ages between 4 and 12 years old), and adolescent group (age > 12 years). Age, gender, time of onset and laterality were investigated. Endoscopic ear examinations were performed to rule out external and/or middle ear diseases that could cause hearing impairment. Pure tone audiometry and speech audiometry were carried out in all patients to evaluate their hearing loss. Furthermore, following tests were reviewed to exclude patients with possible secondary causes of hearing loss: complete blood count (CBC), blood urea nitrogen (BUN), creatinine, urine analysis, antinuclear antibody (ANA), rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), thyroid-stimulating hormone (TSH), free thyroxine (FT4), and rapid plasma reagin (RPR). Inner ear magnetic resonance imaging (MRI) was performed in most patients to exclude middle ear diseases and inner ear malformations. The inclusion criteria of patients enrolled in this study were as follows: (1) diagnosed with SSHNL according to the criteria defined in "Clinical Practice Guideline: Sudden Hearing Loss"[1]; (2) aged ≤ 19 years old; (3)

underwent early therapeutic management, begun before 2 weeks, and (4) had follow-up duration longer than 1 month. Exclusion criteria were patients: (1) aged under 4 years; (2) who had middle ear or retro-cochlear pathology; (3) who had a history of Meniere disease, autoimmune hearing loss or radiation-induced hearing loss; (4) who had a history of genetic hearing loss; (5) who had evidence of acute or chronic otitis media upon examination; or (6) who had a history of otologic surgery. This study was approved by the institutional review board of Seoul National University Boramae Medical Center (permit no.16–2016-144).

Audiometric Assessment

The patients were evaluated using standard methods for examining pure tone thresholds. The standard audiometric protocol involved examining pure tone air and bone conduction thresholds at 0.125, 0.25, 0.5, 1, 2, 3, 4 and 8 kHz. Mean pure tone audiograms were calculated at 0.5, 1.0, 2.0, and 3.0 kHz for air conduction thresholds. Four types of audiograms were defined based on the pattern of hearing loss in the initial pure tone audiometry (PTA): ascending (the average threshold of 0.25 to 0.50 kHz was 20 dB higher than the average threshold of 4 to 8 kHz), descending (the average threshold of 4 to 8 kHz was 20 dB higher than the average threshold of 0.25 to 0.50 kHz), flat (similar threshold observed across the all frequency ranges) and profound (the average threshold in 0.5, 1.0, 2.0 and 3.0 kHz over 90 dB HL). Hearing levels were assessed before treatment, and final treatment

outcomes after treatment were measured with audiogram– PTA and speech discrimination scores (SDS) – performed from one to three months after treatment. The hearing gain was calculated as the difference between initial and final hearing levels (PTA). Siegel's criteria[22] were employed to assess treatment results of the subjects (Table 1). According to Siegel's criteria, hearing recovery was defined as complete recovery (CR) and partial recovery (PR), whereas slight recovery (SR) and no improvement (NI) were categorized as no recovery.

Treatment Protocols

All 67 patients were treated with corticosteroids (prednisolone 1 mg/kg/day as initial dose and tapered). Seventeen of these patients underwent additional intratympanic steroid injection for salvage treatment of unimproved hearing after systemic steroid administration.

Statistical Analysis

The data are demonstrated as mean ± standard deviation (SD) to represent the differences between two groups in age, the period between the onset of hearing loss and treatment, and pre- and post- treatment PTAs. Fisher's exact test and Chi-squared test were carried out to evaluate clinical characteristics and possible

prognostic factors. Two-tailed Student t-tests and non-parametric Mann–Whitney U tests were applied to investigate continuous variable prognostic factors. The parameters that were statistically significant in univariate analysis were involved in binary logistic regression analysis for multivariate analysis. All statistical analysis was carried out with SPSS version 22.0 for Windows (IBM, Armonk, NY, USA). A P value <0.05 was considered to be statistically significant.

RESULTS

Patient Characteristics

The age of all 67 patients ranged from 4 to 19 years (mean 14.0 ± 4.1 years). The patients consisted of 40 males and 27 females. All patients had unilateral hearing loss, and the right to left ratio was 40:27. The mean duration between onset of the disease and initiation of treatment was 3.2 days. Tinnitus and vertigo accompanied the onset of SSNHL in 61.2% and 28.4% of patients, respectively. Mean PTA and SDS at initial presentation were 81.0 dB and 17.9%, respectively (Table 2). Age in the childhood group (n = 22) ranged from 4 to 12 years and mean age was 9.1 years. Age in the adolescent group (n = 45) ranged from 13 to 19 years and mean age was 16.4 years. There was no significant difference in demographic, clinical or audiological features between the two groups except for initiation of treatment. The initiation of treatment was significantly later in the childhood group than in the adolescent group ($p < 0.05$) (Table 2).

Treatment Outcomes

The recovery rate (CR + PR according to Siegel's criteria) of all patients was 55.2%. The percentages of patients in each Siegel's grade are shown in Fig. 1. The recovery rate of the adolescent group was higher than that of the childhood group

(*p=0.030*) (Fig. 2). The complete recovery rate was 22.7% and 42.2% in the childhood and adolescent groups, respectively (*p>0.05*) (Fig. 2). The other percentages of patients in PR, SR and NI are seen in Fig. 2. In addition, the childhood group achieved lower hearing gain than the adolescent group (*p=0.007)* (Table 2).

Prognostic factors

Patients were divided into two groups based on the final status of hearing recovery after treatment: recovery and no recovery groups (Table 3). After univariate analysis, patients were significantly older in the recovery group than those in the no recovery group (*p=0.031*). There was no significant difference between these two groups in terms of gender and side of hearing loss. In the recovery group, tinnitus more frequently occurred at the onset of SSNHL (*p=0.007*); however, the incidence of vertigo was not significantly different between the two groups (*p>0.05*). Moreover, the recovery group involved more patients with descending type audiograms than the no recovery group (*p=0.029*). Treatment was started earlier in the recovery group compared to the no recovery group, although not to a statistically significant degree. There was no significant difference in outcome between intravenous dexamethasone and oral corticosteroid treatment. In addition, intratympanic dexamethasone injections had no significant effect on prognosis. Parameters that were statistically significant in the univariate analysis were

involved in the multivariate analysis. Initial SDS was not included in the multivariate analysis due to close correlation between PTA threshold and SDS. Multivariate analysis showed that initial PTA threshold and presence of tinnitus had a positive correlation with hearing ($p<0.05$) (Table 3). Subgroup analysis revealed different prognostic factors in the childhood and adolescent groups. In the childhood group, initiation of treatment was a significant prognostic factor ($p=0.019$), whereas initial hearing level had no significant effect on prognosis ($p>0.05$) (Table 4). On the other hand, in the adolescent group, initial PTA, initial SDS and salvage intratympanic steroid injection were significant prognostic factors ($p= 0.004$, $p=0.006$ and $p=0.015$, respectively) (Table 5). Cochlear enhancement on MRI was found in 6 patients among 45 patients who had inner ear MRI. There was no significant difference in recovery rate between patients with cochlear enhancement and those without cochlear enhancement ($p=0.399$, Odds ratio = 2.59) (Fig. 3.).

DISCUSSION

SSNHL in children has been uncommonly discussed in the literature, and treatment guidelines in children have not been established.[1] Systemic steroids have become most widely accepted treatment for both adults and children. Steroids are commonly used in form of prednisolone at an initial dose of 1mg/kg and tapered over 2 weeks.[16,21] Recently, Intratympanic steroid injection is frequently used in the treatment of SSNHL. In a systemic review of the literature[18], intratympanic steroids may provide comparable treatment to systemic steroids and could result in additional effect as salvage treatment. Furthermore, some studies reported that higher hearing gain was achieved in patients treated with combined intratympanic and systemic steroids as an initial treatment.[23,24] In contrast to adults, however, there was no significant effect of the combined intratympanic and systemic steroids treatment in children with SSNHL compared to the systemic steroid treatment alone in the study of Övet.[25]

In contrast to SSNHL in adults, treatment outcomes and prognostic factors of SSNHL in children are not well known. The recovery rate of SSNHL in the pediatric population has differed among previous studies. In studies by Byl *et al*.[4] and Li *et al*.[7], the prognosis of children with SSNHL was worse than that of the adult population. However, the treatment outcomes in children with SSNHL were better than adults in a study by Chung *et al*.[21] In our study, the recovery rate of

children with SSNHL was 55.2%, which is similar to that−59.5%− in the study by Chung *et al*.[21] This recovery rate in children was similar to the 52.5% and 59.0% recovery rates demonstrated in the studies of adult populations.[19,26] Considering pediatric developmental stages[27,28], we divided all 67 patients into two groups: childhood group (age between 4 and 12 years old) and adolescent group (age > 12 years). Patients aged less than 4 years were excluded, because it is very difficult to detect SSNHL at an early stage. When dividing these patients in the present study into childhood and adolescent groups, the recovery rate-36.4%- of the childhood group was much lower than those-52.5% and 59.0%- in adults in other studies[19,26] as well as that-64.4%- of the adolescent group. Therefore, we analyzed clinical characteristics of the childhood and adolescent groups to identify possible factors that could have induced different treatment outcomes. There was no difference in clinical features including initial hearing level and associated symptoms between the childhood and adolescent groups except for initiation of treatment ($p=0.048$). Initiation delay of treatment after onset of SSNHL has been considered to be an important prognostic factor.[4,18] The mean duration to the initiation of treatment after onset of disease was different between the two groups in this study. The childhood group had a later initiation of treatment than the adolescent group (4.6 and 2.4 days, respectively). The reason for the delay in the childhood group is not clear, but it is likely that one of the main reasons is that younger children have more difficulty expressing hearing loss. Since SSNHL is rare in young children, moreover, primary physician could misdiagnose childhood patients with SSNHL as

other causes of hearing loss including middle ear effusion which is the most common cause of acquired hearing loss in childhood. This delay in treatment seems to be a cause of the low recovery rate in the childhood group. Another reason for the low recovery rate in the childhood group may be undetected congenital hearing loss. Even though we excluded patients who had a vague onset of hearing loss or newly detected inner ear disease, congenital hearing loss cannot be ruled out completely due to decreased ability of younger children to express hearing loss expression of hearing loss in the childhood group. It is not unusual that unilateral hearing loss goes undetected until screening in schools; this occurrence reveals a lack of recognition of congenital hearing loss in children.[29] Therefore, there is a possibility that patients in the childhood group who had no response to steroids had congenital hearing loss but had been misdiagnosed as SSNHL. When considering late diagnosis and the low recovery rate of SSNHL in childhood, younger children who present with sudden-onset hearing loss should be assessed very carefully with detailed history taking and diagnostic work-up. Once a child is diagnosed with SSNHL, active treatment is required immediately.

The present study suggests age, initial hearing threshold, speech performance scores before treatment, descending type audiogram and coexistence of tinnitus as prognostic factors in univariate analysis. Age of the recovery group was significantly higher than that of the no recovery group (15.0 and 12.8 years, respectively), which is consistent with the difference in recovery rate between the childhood and adolescent groups. In addition, better initial hearing was correlated

with better outcome, which was consistent with previous studies.[15,21] Presence of tinnitus has been correlated with favorable outcomes in various studies of pediatric and adult populations.[21,30,31] In a study of Hikita-Watanabe *et al*[31], tinnitus is considered as an essential factor for cell survival rather than a sign for poor prognosis in SSNHL. It was demonstrated by Kitahara and Balaban that high-dose salicylate which causes reversible tinnitus could up-regulate brain-derived neurotrophic factor (BDNF) in the inner ear for cell survival and induce subsequent transcription of transient receptor potential cation channel superfamily V type 1 (TRPV1) in the inner ear to generate tinnitus[32,33]. In our study, tinnitus was a positive prognostic factor for hearing recovery, which was consistent with previous studies. In several studies of SSNHL, vertigo has been reported as a negative prognostic factor for hearing recovery.[4,18] The presence of vertigo might imply a large extent of damage in the labyrinth, which can correlate with severity of cochlear damage.[34] In contrast to SSNHL in adults, vertigo was not a predictive factor in the present study or in current studies in pediatric populations, which suggests different etiologies of SSNHL in children and adults.[7,21] In contrast to a previous study,[7,21] there was no significant difference in initiation of treatment between the recovery group and the no recovery group (2.6 and 3.9 days, respectively, *p=0.191*). Subgroup analysis revealed that early initiation of treatment was a significant prognostic factor in the childhood group *(p=0.019*). However, the mean duration to the initiation of treatment after onset of disease was not a significant prognostic factor in the adolescent group (*p=0.294*). Instead, treatment

outcomes in adolescence were significantly influenced by initial hearing level. It is suspected that in the 45 patients in the adolescent group, none had difficulty expressing their hearing loss and underwent early initiation of treatment; duration to the initiation of treatment after onset of disease was not significantly different among them. Since more than two-thirds of patients were included in the adolescent group, it seems that initiation of treatment was not a significant prognostic factor in all enrolled patients. In a subgroup analysis of the childhood group, initial hearing threshold level was lower in the recovery group, but not to a statistically significant degree (74.4 and 87.5 dB in the recovery and the no recovery groups, respectively, $p=0.217$). These results could be attributed to the small number of patients in the childhood group. In a subgroup analysis of the adolescent group, intratympanic steroid injection was more frequently performed in the no recovery group. It seems that, rather than being a prognostic factor, intratympanic steroid injection may have been used as a salvage treatment in patients with poor treatment outcomes. Multivariate analysis revealed initial PTA threshold and presence of tinnitus had a positive relation to hearing recovery ($p<0.05$). Although statistical significance was not met, older age children tended to exhibit better outcomes ($p=0.055$). A study with a large population is required to confirm the correlation between patients' age and prognosis. Since we excluded patients who had retro-cochlear lesions or congenital hearing loss, no pathologic finding was identified in MRI except cochlear enhancement. Cochlear enhancement on MRI is considered as a sign of inner ear inflammation and is

found in 3.8% to 9% of patients with SSNHL.[18] In our study, cochlear enhancement was found in 13% of patients, and recovery rates were not significantly different between patients with cochlear enhancement and those without cochlear enhancement (*p=0.399*, Odds ratio=2.59). Because there were only six patients who showed cochlear enhancement on MRI, a study with a larger population should be conducted to identify correlation between cochlear enhancement and prognosis.

To the best of our knowledge, this study is the first study about pediatric SSNNL which focused on age as a prognostic factor. The strength of our study is that it was performed with relative large pediatric population and strict inclusion criteria which included treatment started within 2 weeks from onset of SSNHL with definite dosage of systemic steroid (an initial dose of prednisolone 1mg/kg and tapered). However, the present study has some limitations. The main limitations in our study are that it was retrospective in nature, and the number of participants was smaller than those in the studies of SSNHL in adult populations due to the low incidence of SSNHL in the pediatric population. In addition, intratympanic steroid injection was more frequently performed in the adolescent group than the childhood group, because most patients in the childhood group did not tolerate intratympanic steroid injection (2/22 in the childhood group and 17/45 in the adolescent group, respectively, *p=0.039,* data not shown). Even though intratympanic steroid injections had no significant effect on prognosis in the present study, the potential benefits of intratympanic steroid injection could have

effect on different prognosis between the childhood and adolescent groups. Therefore, further investigation should be performed with a consistent treatment protocol for childhood and adolescent patients. Even though 71.6% (48/67) of final audiograms were performed at three months after initiation of treatment, 19 patients (28.4%) did not undergo their audiogram at that time. Hearing recovery in these 19 patients could be underestimated, because they did not have sufficient time for recovery compared to the other 48 patients. However, it was reported that 92.4% of hearing recovery was achieved within posttreatment 5 weeks and only 6.5% of hearing recovery was accomplished between posttreatment 5 weeks and 3 months in the study of Yeo *et al*[35]. Among these 19 patients, in addition, only three patients were involved in no recovery group, which indicates 4.5% (3/67) of patients did not have adequate time for recovery. It is assumed that more patients in the recovery group did not visit clinic at three months due to improvement of their symptoms compared to those in the no recovery group. Furthermore, there was no significant difference in number of patients who received final audiogram 1 or 2 months after treatment between the childhood and adolescent groups (4/22 in the childhood group and 15/45 in the adolescent group, $p=0.255$, data not shown), and the mean time of final audiogram between the two groups had no statistical significance (2.6 months and 2.4 months in the childhood and adolescent groups respectively, $p=0.332$, data not shown). It is considered that higher recovery rate in the adolescent group was associated with fewer patients who visited clinic at three months, but the mean follow-up time of final audiogram was not significantly

different between the two groups. Since data on the spontaneous hearing recovery of SSNHL in children is limited, efficacy of treatments including systemic steroid and intratympanic steroid injection are not established. Furthermore, there is no consensus on pediatric dosage of systemic steroids in children with SSNHL, although the present study applied systemic steroids at an initial dose of prednisolone 1mg/kg which is commonly used in adults. Therefore, further studies on treatment of SSNHL in children are required to establish treatment guidelines.

CONCLUSSION

Among SSNHL patients in a pediatric population, children aged 12 years or below had lower recovery rates than children above 12 years of age. In addition, high initial hearing threshold and absence of tinnitus were negatively associated with hearing recovery. These prognostic factors can be helpful to predict treatment outcomes in pediatric patients with SSNHL, and active treatment is required for patients with poor prognostic factors. Furthermore, because of worse prognosis and a possibility of congenital hearing loss in pediatric patients with SSNHL, it might be necessary that children presenting with sudden-onset hearing loss should be evaluated very carefully with detailed history taking and diagnostic work-up.

REFERENCES

1. Stachler RJ, Chandrasekhar SS, Archer SMet al. Clinical practice guideline sudden hearing loss. Otolaryngology--Head and Neck Surgery 2012; 146:S1-S35.
2. Alexander TH, Harris JP. Incidence of sudden sensorineural hearing loss. Otology & Neurotology 2013; 34:1586-1589.
3. Klemm E, Deutscher A, Mösges R. [A present investigation of the epidemiology in idiopathic sudden sensorineural hearing loss]. Laryngo-rhino-otologie 2009; 88:524-527.
4. Byl FM. Sudden hearing loss: eight years' experience and suggested prognostic table. The Laryngoscope 1984; 94:647-661.
5. Ottaviani F, Cadoni G, Marinelli Let al. Anti-endothelial autoantibodies in patients with sudden hearing loss. The Laryngoscope 1999; 109:1084-1087.
6. Debry C, Grandjean E, Briche D, El Jerrari A, Gentine A, Contraux C. Surdités brusques: analyse d'une série de 117 cas *Annales d'oto-laryngologie et de chirurgie cervico-faciale*: Elsevier Masson, 1992:175-181.
7. Li F-J, Wang D-Y, Wang H-Yet al. Clinical Study on 136 Children with Sudden Sensorineural Hearing Loss. Chinese medical journal 2016; 129:946.
8. Chau JK, Lin JR, Atashband S, Irvine RA, Westerberg BD. Systematic review of the evidence for the etiology of adult sudden sensorineural hearing loss. The Laryngoscope 2010; 120:1011-1021.
9. Tarshish Y, Leschinski A, Kenna M. Pediatric sudden sensorineural hearing loss: diagnosed causes and response to intervention. International journal of pediatric otorhinolaryngology 2013; 77:553-559.
10. Mattox DE, Simmons FB. Natural history of sudden sensorineural hearing loss. Annals of Otology, Rhinology & Laryngology 1977; 86:463-480.
11. Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of

idiopathic sudden hearing loss: a double-blind clinical study. Archives of Otolaryngology 1980; 106:772-776.

12. Chandrasekhar SS. Intratympanic dexamethasone for sudden sensorineural hearing loss: clinical and laboratory evaluation. Otology & neurotology 2001; 22:18-23.
13. Haynes DS, O'Malley M, Cohen S, Watford K, Labadie RF. Intratympanic dexamethasone for sudden sensorineural hearing loss after failure of systemic therapy. The Laryngoscope 2007; 117:3-15.
14. Guan-Min H, Hung-Ching L, Min-Tsan S, Cheng-Chien Y, Hsun-Tien T. Effectiveness of Intratympanic Dexamethasone Injection in Sudden-Deafness Patients as Salvage Treatment. The Laryngoscope 2004; 114:1184-1189.
15. Roman S, Aladio P, Paris J, Nicollas R, Triglia J-M. Prognostic factors of sudden hearing loss in children. International journal of pediatric otorhinolaryngology 2001; 61:17-21.
16. Moon YE, Yang SD, Choi JCet al. Clinical Characteristics and Treatment Results of Sudden Deafness in Children. Korean Journal of Otorhinolaryngology-Head and Neck Surgery 2009; 52:805.
17. Chon KM, Goh EK, Lee IW, Cho KS. Clinical observation of sudden deafness in children. Korean Journal of Otolaryngology-Head and Neck Surgery 2002; 45:456-461.
18. Kuhn M, Heman-Ackah SE, Shaikh JA, Roehm PC. Sudden sensorineural hearing loss: a review of diagnosis, treatment, and prognosis. Trends in amplification 2011:1084713811408349.
19. Kim S, Jung S, Kim M, Byun J, Park M, Yeo S. Comparison of steroid administration methods in patients with idiopathic sudden sensorineural hearing loss: a retrospective observational study. Clinical Otolaryngology 2015; 40:183-190.
20. Kim YH, Park KT, Choi BYet al. Early combination treatment with intratympanic steroid injection in severe to profound sudden sensorineural hearing loss improves speech discrimination performance. European Archives of Oto-Rhino-Laryngology 2012; 269:2173-2178.

21. Chung JH, Cho SH, Jeong JH, Park CW, Lee SH. Multivariate analysis of prognostic factors for idiopathic sudden sensorineural hearing loss in children. The Laryngoscope 2015; 125:2209-2215.
22. Siegel L. The treatment of idiopathic sudden sensorineural hearing loss. Otolaryngologic clinics of North America 1975; 8:467.
23. Battaglia A, Burchette R, Cueva R. Combination therapy (intratympanic dexamethasone+ high-dose prednisone taper) for the treatment of idiopathic sudden sensorineural hearing loss. Otology & Neurotology 2008; 29:453-460.
24. Battaglia A, Lualhati A, Lin H, Burchette R, Cueva R. A prospective, multi-centered study of the treatment of idiopathic sudden sensorineural hearing loss with combination therapy versus high-dose prednisone alone: a 139 patient follow-up. Otology & Neurotology 2014; 35:1091-1098.
25. Övet G, Alataş N, Güzelkara F. Sudden Pediatric Hearing Loss: Comparing the Results of Combined Treatment (Intratympanic Dexamethasone and Systemic Steroids) With Systemic Steroid Treatment Alone. Otology & neurotology: official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 2016.
26. Yeo SW, Lee DH, Jun BC, Park SY, Park YS. Hearing outcome of sudden sensorineural hearing loss: long-term follow-up. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 2007; 136:221-224.
27. Kliegman S. St Geme. Schor Nelson Textbook of Pediatrics, 20th Edition, Saunders Elsevier 2015.
28. Shephard RJ. Physical activity, health, and well-being at different life stages. Research quarterly for exercise and sport 1995; 66:298-302.
29. Bess FH, Tharpe AM. Unilateral hearing impairment in children. Pediatrics 1984; 74:206-216.
30. Danino J, Joachims H, Eliachar I, Podoshin L, Ben-David Y, Frandis M. Tinnitus as a prognostic factor in sudden deafness. American journal of

otolaryngology 1984; 5:394-396.

31. Hikita-Watanabe N, Kitahara T, Horii A, Kawashima T, Doi K, Okumura S-I. Tinnitus as a prognostic factor of sudden deafness. Acta oto-laryngologica 2010; 130:79-83.
32. Kitahara T, Kizawa K, Horii A, Kubo T, Balaban C. Changes in TRPV1 expression in the rat auditory pathway after salicylate challenge *36th Neuroscience Meeting, Atlanta*, 2006.
33. Kitahara T, Li H-S, Balaban CD. Changes in transient receptor potential cation channel superfamily V (TRPV) mRNA expression in the mouse inner ear ganglia after kanamycin challenge. Hearing research 2005; 201:132-144.
34. Nakashima T, Yanagita N. Outcome of sudden deafness with and without vertigo. The Laryngoscope 1993; 103:1145-1149.
35. Yeo S-W, Lee D-H, Jun B-C, Park S-Y, Park Y-S. Hearing outcome of sudden sensorineural hearing loss: long-term follow-up. Otolaryngology--Head and Neck Surgery 2007; 136:221-224.

Grade	Hearing recovery
I. Complete recovery (CR)	Final hearing level was less than 25 dB
II. Partial recovery (PR)	Final hearing from 25 to 45 dB with hearing gain of ≥15 dB
III. Slight recovery (SR)	Final hearing over 45 dB with hearing gain of ≤15 dB
IV. No improvement (NI)	Final hearing level over 75 dB with hearing gain of ≤15 dB

Table 1. Siegel's criteria of hearing recovery

	Childhood group	Adolescent group	Total patients	
	n = 22	n = 45	N = 67	P Value
Age (years)	9.1±2.4	16.4±2.1	14.0±4.1	
Gender, male : female	11:11	29:16	40:27	0.258*
Side of SNHL, right : left	16:6	26:19	42:25	0.235*
Initiation of treatment (days)	4.6±4.6	2.4±2.9	3.2±3.7	**0.048**†∪
Accompanying symptoms				
Tinnitus	50.0% (11/22)	66.7% (30/45)	61.2% (41/67)	0.189*
Vertigo	27.3% (6/22)	28.9% (13/45)	28.4% (19/67)	0.890*
Audiometry				
Initial hearing level, PTA (dB)	82.7±23.6	80.2±24.4	81.0±24.0	0.686‡
Initial Speech discrimination score (%)	15.8±26.3	19.0±30.9	17.9±4.0	0.589∪
Recovery rate	36.4% (8/22)	64.4% (29/45)	55.2% (37/67)	**0.030**†*
Hearing gain, PTA (dB)	27.9±24.3	46.3±25.5	40.2±26.4	**0.007**†‡

*Pearson chi-squared test

‡Student t test

∪Mann Whitney U-test

†Bold text indicates statistical significance (P<0.05).

Table 2. Clinical characteristics and recovery rate in childhood (age ≤ 12 years) and adolescent (age > 12 years) groups

	Recovery	No recovery	Univariate	Multivariate			
	(n = 37)	(n = 30)	P Value	P Value	B	SE	Exp(B)
Age (years)	15.0±3.2	12.8±4.7	**0.031**[†‡]	0.055	-0.151	0.079	0.86
Gender, male : female	24:13	16:14	0.339[*]				
Side of SNHL, right : left	24:13	18:12	0.682[*]				
Initiation of treatment (days)	2.6±2.8	3.9±4.4	0.191[‡]				
Accompanying symptoms							
Tinnitus	75.7% (28/37)	43.3% (13/30)	**0.007**[†*]	**0.014**[†§]	1.51	0.615	4.529
Vertigo	24.3% (9/37)	33.3% (10/30)	0.416[*]				
Audiometry							
Initial hearing level, PTA (dB)	73.0±24.3	90.9±20.0	**0.002**[†‡]	**0.003**[†§]	0.039	0.013	1.04
Initial Speech discrimination score (%)	26.6±35.6	7.2±12.7	**0.003**[†‡]				
Hearing gain, PTA (dB)	53.9±24.4	23.4±17.6	**<0.001**[†‡]				
Type of audiogram							
Ascending	3 (8.1%)	2 (6.7%)	1.000[¶]				
Descending	6 (16.2%)	0 (0%)	**0.029**[†¶]				
Flat	16 (43.2%)	13 (43.3%)	0.994[*]				
Profound	12 (32.4%)	15 (50.0%)	0.145[*]				
Treatments							
Intravenous : oral steroid	23:14	14:16	0.205[*]				
Salvage intratympanic steroid injection	18.9% (7/37)	33.3% (10/30)	0.178[*]				

[*]Pearson chi-squared test, [¶]Fischer′s exact test

[‡]Student t test.

[§]Binary logistic regression analysis.

[†]Bold text indicates statistical significance (P<0.05).

#Both initial pure tone audiometry threshold and speech discrimination are parameters of hearing level; initial pure tone audiometry threshold was included in the multivariate analysis.
B = Standardized Coefficient; Exp(B) = odds ratio; SE = standard error;

Table 3. Prognostic factors in all enrolled patients

	Recovery (n = 8)	No Recovery (n = 14)	P Value
Age (years)	10.3±1.8	8.5±2.5	0.127‡
Gender, male : female	3:5	8:6	0.659¶
Side of SNHL, right : left	5:3	11:3	0.624¶
Initiation of treatment (days)	2.0±2.6	6.1±4.9	**0.019**†∪
Accompanying symptoms			
Tinnitus	75.0% (6/8)	35.7% (5/14)	0.183¶
Vertigo	25.0% (2/8)	28.6% (4/14)	1.000¶
Audiometry			
Initial hearing level, PTA (dB)	74.4±29.5	87.5±19.0	0.217‡
Initial Speech discrimination score (%)	27.5±37.9	9.1±14.4	0.330∪
Hearing gain, PTA (dB)	48.5±24.5	16.2±14.9	**0.006**†∪
Treatments			
Intravenous : oral steroid	5:3	8:6	1.000¶
Salvage intratympanic steroid injection	12.5% (1/8)	7.1% (1/14)	1.000¶

*Pearson chi-squared test, ¶Fischer′s exact test

‡Student t test.

∪Mann Whitney U-test

†Bold text indicates statistical significance (P<0.05).

Table 4. Prognostic factors in childhood group (age ≤ 12 years)

	Recovery (n = 29)	No Recovery (n = 16)	P Value
Age (years)	16.3±2.1	16.6±2.1	0.737‡
Gender, male : female	21:8	8:8	0.133*
Side of SNHL, right : left	19:10	7:9	0.157*
Initiation of treatment (days)	2.8±2.9	1.8±2.7	0.294‡
Accompanying symptoms			
Tinnitus	75.9% (22/29)	50.0% (8/16)	0.078*
Vertigo	24.1% (7/29)	37.5% (6/16)	0.344*
Audiometry			
Initial hearing level, PTA (dB)	72.6±23.4	93.9±20.6	**0.004**†‡
Initial Speech discrimination score (%)	26.4±35.7	5.5±11.3	**0.011**†∪
Hearing gain, PTA (dB)	55.4±24.6	29.7±17.8	**0.001**†‡
Treatments			
Intravenous : oral steroid	18:11	6:10	0.114*
Salvage intratympanic steroid injection	20.7% (6/29)	56.3% (9/16)	**0.015**†*

*Pearson chi-squared test

‡Student t test.

∪Mann Whitney U-test

†Bold text indicates statistical significance (P<0.05).

Table 5. Prognostic factors in adolescent group (age > 12 years)

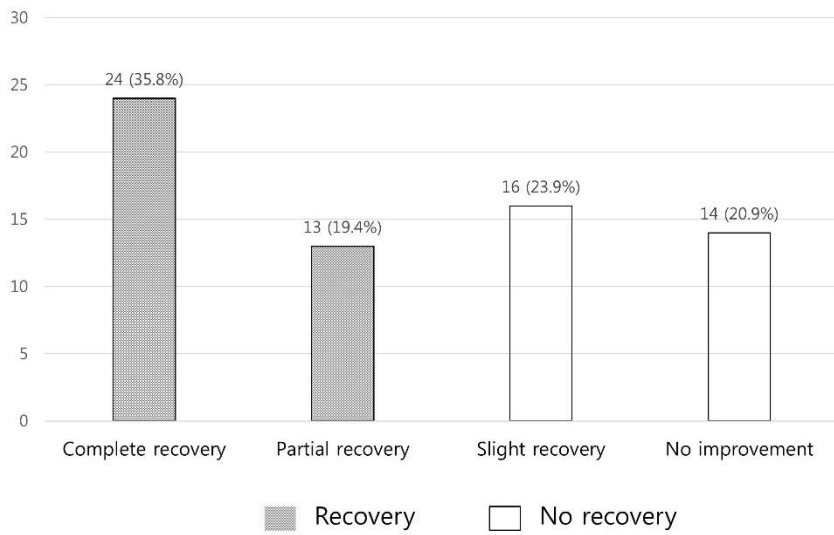

Fig. 1. Comparison of posttreatment outcomes by Siegel's criteria in all patients (n = 67). Percentages of patients in complete recovery, partial recovery, slight recovery, and no improvement were 35.8%, 19.4%, 23.9%, and 20.9%, respectively. Recovery rate (complete recovery and partial recovery) was 55.2%.

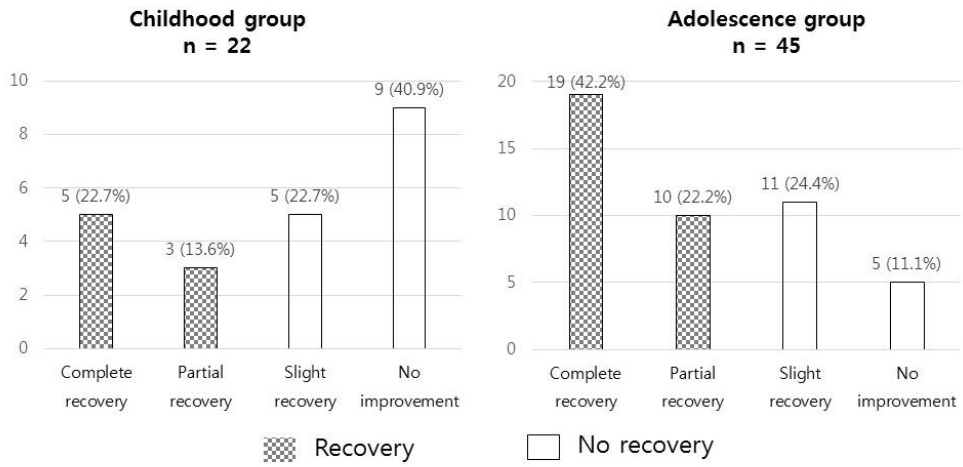

Fig. 2. Comparison of posttreatment outcomes by Siegel's criteria in childhood (age ≤ 12 years) and adolescent (age > 12 years) groups. Recovery rates in each group were 36.3% and 64.4%, respectively.

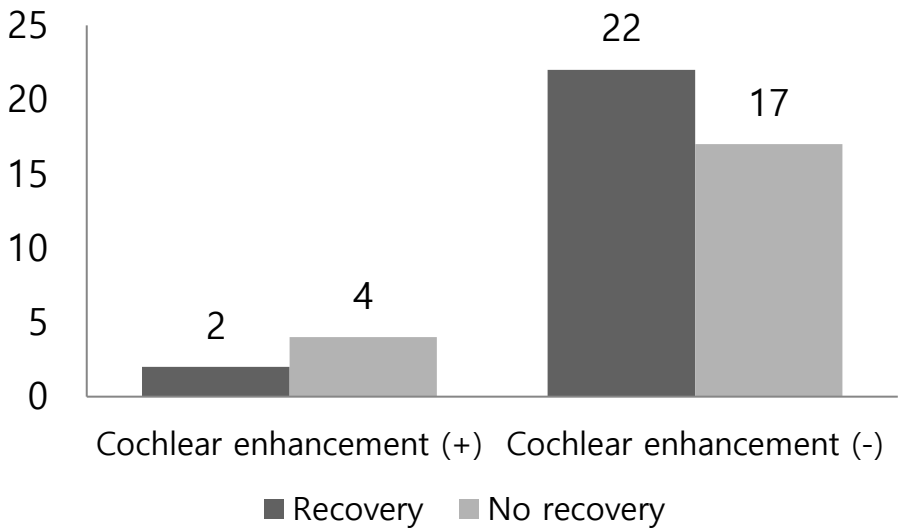

Fig. 3. Comparison of recovery rates according to cochlear enhancement on MRI (n = 45). Recovery rates in patients with cochlear enhancement and those without cochlear enhancement were 33.3% and 56.4%, respectively.

국문초록

서론: 돌발성 난청은 현재까지 많은 연구가 진행되고 있으나 소아에서 발생한 경우에 관해 알려진 바가 적어 치료 후 예후에 대한 연구의 필요성이 있다. 본 연구는 소아 돌발성 난청의 임상 특성, 치료결과 및 예후에 대해 분석하고자 한다.

재료 및 방법: 2005년 1월부터 2016년 6월까지 서울의대 3개 병원에서 돌발성 난청으로 진단된 19세 이하 67명의 환자들을 대상으로 임상양상과 청력검사결과 등을 수집하여 후향적으로 분석하였다. 환자들은 Steroid 투여(경구 또는 정맥 내, 1mg/kg)를 받았고 17명의 환자들에서는 고실 내 주입(5mg/mL, 4회)을 받았다. 치료 후 청력의 평가는 Siegel's criteria에 따라 시행하였고, 회복기준은 complete recovery 및 partial recovery까지로 하였다. 전체 환자를 아동군(4~12세)과 청소년군(>12세)으로 구분하여 임상적 특징 및 치료 효과 등을 조사하였다. 더불어 청력회복에 따라 환자를 두 군으로 분류하여 가능한 예후 인자들에 대해 평가하였다.

결과 : 전체 소아의 청력회복률은 55.2%로 나타났다. 아동군에서 회복률은 청소년군의 회복률보다 유의하게 낮았다. ($p = 0.030$). 현훈이 동반된 경우와 난청 회복률과의 유의미한 관련성은 없었으나($p = 0.430$) 이명이 동반된 경우 난청 회복률이 의미 있게 높았다($p = 0.007$). 치료 전 청력검사결과에서 낮은 청력역치($p = 0.002$), 높은 어음 명료도($p = 0.003$)와 하강형 청력도($p = 0.029$)가 청력 회복과 양의 상관관계가 있었다. Steroid의 투약 방법과 예후 사이에 유의미한 관계는 없었으며 ($p = 0.205$). 고실 내 주입 여부는 치료 결과에 유의한 영향을 끼치지 않는 것으로 나타났다 ($p = 0.187$). 자기공명영상을 시행 받은 45명의 환자 중 6명에서 와우의 조영증강이 나타났다.

결론 : 아동군은 청소년군에 비해 더 불량한 치료 결과를 가졌다. 높은 초기 청력역치와 이명이 동반되지 않을 경우는 청력 회복에 불량한 예후 인자로 나타났다. 따라서 아동기 소아에서의 돌발성 난청이나 불량한 예후 인자가 동반된 소아의 돌발성 난청에서는 적극적인 치료가 필요할 것으로 사료된다.

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주요어: 돌발성 난청, 소아, 나이, 예후

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